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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,103	04/12/2001	Aki Kitagawa	12372-002001	5320

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EXAMINER	
LEWIS, PATRICK T	
ART UNIT	PAPER NUMBER
1623	9

DATE MAILED: 07/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/834,103	Applicant(s) KITAGAWA ET AL.	
	Examiner Patrick T. Lewis	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *1-11 and 23-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Priority

1. Acknowledgment is made of applicant's claim for foreign priority based on applications filed in Japan on April 17, 2000 and July 5, 2000. It is noted, however, that applicant has not filed certified copies of the JP 2000-115091 and JP 2000-203850 applications as required by 35 U.S.C. 119(b).

Election/Restrictions

2. Applicant's election without traverse of Group II (claims 12-25) in Paper No. 8 is acknowledged.

Specification

3. The abstract of the disclosure is objected to because the title "Sustained Release Drug Composition" should be removed. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 12-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki et al. EP 0 913 149 A1 (Suzuki) in view of Igari et al US 5,344,644 (Igari).

Claims 12-25 are drawn to a method of producing a sustained release drug composition comprising providing a precipitating solution containing a mucopolysaccharide, a carrier protein, and a drug; lowering the pH of the solution to form an insoluble product; and collecting from the solution the insoluble product.

Suzuki discloses drug compositions with controlled drug release rates (page 2, lines 35-49). The compositions comprise a matrix formed from (**a**) and (**b**), wherein (**a**)

is a biodegradable, biocompatible high-molecular substance and/or polyvalent metal ions or polyvalent metal ion source and (**b**) is hyaluronic acid or a salt thereof; and a drug (**c**) (page 2, lines 35-49). Examples of biodegradable, biocompatible high-molecular substances include gelatin, sodium casein, albumin, and lysozyme chloride (page 3, lines 11-17). Preferred polyvalent ions include Ca^{2+}, Al^{3+}, and Fe^{3+} (page 3, lines 16-19). A wide variety of drugs may be used including but not limited to anti-inflammatory drugs, hypnotic sedatives, stimulants, ophthalmic drugs, cardiacs, diuretics, antibiotics, antitumor agents, chemotherapeutic agents, and vitamins (page 3, lines 33-48). The content of ingredient (**a**) in the composition may range from 5 to 95 wt.% (page 3, lines 23-24). The content of ingredient (**b**) may range from 50 to 80 wt.% (page 3, lines 45-48). The composition may further comprise excipients, stabilizers, preservatives, surfactants, buffers and the like (page 4, lines 10-11).

Suzuki teaches a submerged hardening method for producing the composition (page 4, lines 37-49). According to the method, a solution of the hyaluronic acid or salt thereof (**b**) is added to a hydrophobic solvent and emulsified. The formed emulsion is then added under stirring to a solution of a biodegradable, biocompatible high-molecular substance and/or polyvalent metal ions or polyvalent metal ion source (**a**). After the resulting mixture is stirred, microcapsules are allowed to form. The microcapsules are collected by filtration, washed and then dried, whereby microcapsules are obtained as the drug composition. The drug (**c**) may generally be added beforehand in the solution of (**a**) and/or the solution of (**b**) unless addition of (**c**) in a different manner is required for

its physical and/or chemical properties. Suzuki further teaches the addition of albumin (**a**) in an acidic solution (page 7, Examples 33-34).

Suzuki does not explicitly disclose lowering the pH of the precipitating solution; however, one of ordinary skill in the art would recognize that the addition of an acidic solution would indeed lower the pH of the solution. Suzuki does disclose the use of γ-globulin as a carrier protein. Suzuki does not disclose lyophilizing a preparatory solution with a pH of 6 to 8 to obtain the product.

Igari discloses a method for preparing sustained-release compositions. The compositions comprise a pharmaceutically active agent (column 3, lines 52-59). Pharmaceutically active agents which may be used include interferons (e.g. alpha, beta, gamma), interleukins (e.g. IL-2 to IL-11), erythropoietin, granulocyte colony stimulating factors, granulocyte-macrophage colony stimulating factors, thrombopoietin, insulin, growth hormones, and parathyroid hormone related peptide (columns 3-4). The composition may further comprise a mucopolysaccharide such as chondroitin sulfate, heparin, and keratan sulfate (column 5, lines 16-65). The composition may further comprise water-soluble proteins such as serum albumin, globulin, collagen, or gelatin (column 6, lines 7-15). The weight ratio between the water-soluble protein and the mucopolysaccharide is 0.00001:1 to 100:1 (column 6, lines 16-23). Igari teaches that the lowering the pH of a composition below 4 will cause the formation of a precipitate (column 6, lines 43-52). Igari also teaches that the composition may be in a form dissolved in water or in a lyophilized form (column 7, lines 31-33). The compositions

may be made by admixing the ingredients using conventional methods (column 7, lines 56-68).

It would have been obvious to one of ordinary skill in the art at the time of the invention to lower the pH of the preparatory solution as described by Suzuki below 4 since Igari teaches that lowering the pH causes precipitation. It would have also been obvious to one of ordinary skill in the art to use γ-globulin as a carrier protein since Igari teaches the use globulins (also teaches serum albumin, collagen, and gelatin) as carrier proteins for forming sustained-release compositions. Igari also teaches that the composition may be in a lyophilized form. Being that Igari and Suzuki teach very similar compositions it would have been obvious to the skilled artisan that composition as disclosed by Suzuki may also be in a lyophilized form. Modifications of Suzuki to obtain the instantly claimed invention are seen to be a choice of experimental design and would have been well within the purview of the skilled artisan in the field.

Conclusions

8. Claims 1-46 are pending. Claims 1-11 and 26-46 are drawn to a non-elected invention. Claims 12-25 are rejected. No claims are allowed. References cited but not used in an art rejection are provided to show the state of the art.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 703-305-4043. The examiner can normally be reached on M-F 8:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 703-308-4532. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Patrick T. Lewis
Examiner
Art Unit 1623

JOHANN RICHTER, PH.D., ESQ.
SUPERVISORY PATENT EXAMINER
GROUP 1600

ptl
July 18, 2002